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| 10/506,335 | 09/02/2004 | Eiko Kato | Q68931 | 8830 |

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| EXAMINER | |
|---|---|
| GULLEDGE, BRIAN M | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/506,335 | KATO ET AL. | |
| | Examiner | Art Unit | |
| | Brian Gulledge | 1619 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2,3 and 7-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3 and 7-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Change of Examiner*

This application has been reassigned from Juné Rogers to Brian Gulledge for the remainder of its prosecution. Applicant is advised that future communications should be directed to Brian Gulledge, who can be contacted at 571-270-5756, Monday–Thursday from 6:00 am until 3:00 pm.

### *Previous Rejections*

Applicants' arguments, filed December 30, 2008, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### *Priority*

This application claims benefit to provisional application No. 60/363,102, filed on March 12, 2002, in a language other than English. An English translation of the non-English language provisional application and a statement that the translation is accurate must be filed in provisional application No. 60/363,102. See 37 CFR 1.78(a)(5). The English translation and the statement that the translation is accurate required by 37 CFR 1.78(a)(5) are missing. Accordingly, applicant must supply 1) the missing English translation and a statement that the translation is accurate in provisional application No. 60/363,102 and 2) in the present

application, a confirmation that the translation and statement were filed in the provisional application. If 1) and 2) are not filed (or the benefit claim withdrawn by the filing of an amendment or Supplemental Application Data Sheet) prior to the expiration of the time period set in this Office action, the present application will be abandoned. See 37 CFR 1.78(a)(5)(iv).

It is noted that this application appears to claim subject matter disclosed in prior Application No. PCT/JP03/02646, filed March 6, 2003. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, a petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 15-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing the amount of pigmentation of the skin, does not reasonably provide enablement for prevention of pigmentation of the skin.** The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v. Guardian,* 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the quantity of experimentation necessary, (2) the amount of direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). While the Examiner has considered all of these factors, a

sufficient amount for a *prima facie* case are discussed below.

*The nature of the invention, state and predictability of the art, and relative skill level:* The invention relates to prevention of pigmentation of the skin. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art.

*The breadth of the claims:* Since the instant specification provides no limiting definition of the term "prevention", the term will be interpreted expansively. The term "prevention" may vary widely in meaning, but encompassed within the definition is prevention of the condition from occurring and preventing it from progressing. Nor is the term limited by any time frame.

The claims are thus very broad insofar as they suggest that one will not experience pigmentation when taking the claimed agent; that should one be exposed to either a light source that can cause pigmentation or a chemical agent that increases the pigment of the skin, that the skin will not increase in pigmentation; or that following its treatment, it will not occur. While such "prevention" might theoretically be possible under strictly controlled laboratory conditions, as a practical matter it is nearly impossible to achieve in the "real world" in which patients live.

*The amount of direction or guidance provided and the presence or absence of working examples:* The specification provides no direction or guidance for practicing the claimed invention in its "full scope". No reasonably specific guidance is provided concerning useful therapeutic protocols for prevention, other than the reduction in the amount of pigmentation as compared to what would otherwise occur. The latter is corroborated by the working examples.

*The quantity of experimentation necessary:* Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the

assertion that the instantly claimed agents could be predictably used to prevent pigmentation of the skin as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the claimed invention in its "full scope" a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

*Suggested alternative language:* Since the term "reducing" is inclusive of various administrative timing schemes and thus provides adequate coverage for all reasonably successful therapies, the examiner recommends deleting the term "preventing" and simply reciting "reducing" instead.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

**Claims 2-3, 7-8, and 11-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Takata et al. (*Journal of Lipid Research*, 2002, 43, pages 2196-2204).** Takata et al. discloses *N,N*-dimethylglycinate of d-γ-tocopherol as a prodrug for d-γ-tocopherol (abstract, lines 1-8). Takata et al. further discloses a solution comprising 5 wt% of the agent (page 2197, last paragraph, lines 3-4). Thus, the subject matter of instant claims 2-3, 7-8, and 11-14 are anticipated by Takata et al.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Claims 2-3 and 7-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weber et al. (*Free Rad. & Med.*, 1997, 22(5), pages 761-769) in view of Takata et al. (*J. Pharm. Sci.*, 1995, 84(1), pages 96-100).** Weber et al. teaches compositions of tocopherols that are applied dermally (title). Weber et al. teaches that the topical application of antioxidants is one approach to diminishing oxidative injury, and the composition taught, vitamin E, includes both γ- and δ-tocopherol (page 761, paragraph [2]). Weber et al. further teaches a composition comprising 5% w/v of tocopherols being applied to the skin of rats (page 762, paragraph [6]). Weber et al. also discloses that the acetate derivative of tocopherol has also been used, delivering high concentrations of the agent into the skin (page 767, paragraph [2], lines 1-7). However, Weber et al. does not teach that instantly recited glycinate derivative of tocopherol.

Takata et al. teaches that the acetate esters of tocopherol are commonly used and that the rate-limiting step for bioavailability is the hydrolysis of the acetate ester (page 96, paragraph [2]). Takata et al. then discloses that two other pro-drugs, one of which being the *N,N*-dimethyl glycinate derivative of tocopherol are better substrates for the enzyme that hydrolyzes the pro-drug than the acetate derivative (page 97, paragraph [3]).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made a pro-drug with the *N,N*-dimethyl glycinate pro-moiety taught by Takata et al. with the composition taught by Weber et al. Takata et al. taught

that the *N,N*-dimethyl glycinate pro-moiety is an improvement over that acetate, which is disclosed by Weber et al.

**Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weber et al. (*Free Rad. & Med.*, 1997, 22(5), pages 761-769) in view of Takata et al. (*J. Pharm. Sci.*, 1995, 84(1), pages 96-100) as applied to claim 2 above, and further in view of Yasuaki (JP 62-106005).** Weber et al. in view of Takata et al. teaches all of the limitations of instant claims 15-17 except for the use of the composition to reduce or eliminate pigmentation. Weber et al. did recognize the use of the composition to treat oxidative damage caused by prolonged UV-exposure (page 761, paragraph [1]).

Yasuaki teaches that a vitamin E comprising, externally applied, composition to suppress the formation of melanin (pigment) formation, which occurs after prolonged exposure to UV-light (abstract, lines 1-11).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the composition, taught by Weber et al. in view of Takata et al. to reduce pigmentation. Yasuaki et al. teaches related compositions for this use, and the composition disclosed by Weber et al. in view of Takata et al. is taught to comprise an improved pro-drug to supply vitamin E components when delivered dermally.

**Claims 2-3 and 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burke et al. (*Nutrition and Cancer*, 2000, 38(1), pages 87-97) in view of Takata et al. (*J. Pharm. Sci.*, 1995, 84(1), pages 96-100).** Burke et al. teaches that topical tocopherol acetate

compositions can be used to reduce pigmentation (abstract, lines 1-24). The tocopherols taught by Burke et al. include α-, β-, γ-, and δ-tocopherol (page 87, paragraph [4]). Burke et al. teaches the application of the agent in a lotion comprising 5 wt% of the agent (page 89, paragraph [5]). Burke et al. does not teach the instantly recited pro-drug moiety.

Takata et al. teaches that the acetate esters of tocopherol are commonly used and that the rate-limiting step for bioavailability is the hydrolysis of the acetate ester (page 96, paragraph [2]). Takata et al. then discloses that two other pro-drugs, one of which being the *N,N*-dimethyl glycinate derivative of tocopherol are better substrates for the enzyme that hydrolyzes the pro-drug than the acetate derivative (page 97, paragraph [3]).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made a pro-drug with the *N,N*-dimethyl glycinate pro-moiety taught by Takata et al. with the composition taught by Burke et al. Takata et al. taught that the *N,N*-dimethyl glycinate pro-moiety is an improvement over that acetate, which is disclosed and used by Burke et al.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Gulledge whose telephone number is (571) 270-5756. The examiner can normally be reached on Monday-Thursday 6:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BMG

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612